Claim Listing:

- 1-9. (Cancelled)
- (Currently Amended) A pharmaceutical composition for treating or preventing a disorder 10. or condition selected from autoimmune diseases, rheumatoid arthritis, type I diabetes (recent onset), lupus, inflammatory bowel disease, optic neuritis, psoriasis, multiple sclerosis, polymyalgia rheumatica, uveitis, and vasculitis, acute and chronic inflammatory conditions osteoarthritis, adult Respiratory Distress Syndrome, Respiratory Distress Syndrome of infancy, ischemia reperfusion injury, glomerulonephritis, and chronic obstructive pulmonary disease (COPD) allergic conditions, asthma and atopic dermatitis, inflammation associated with infection, viral inflammation, influenza, hepatitis and Guillian-Barre, chronic bronchitis, chronic or acute tissue, cell, and solid organ transplant rejection, xeno-transplantation, atherosclerosis, restenosis, HIV infectivity (co-receptor usage), and granulomatous diseases, sarcoidosis, leprosy and tuberculosis, and sequelae associated with cancers, multiple myelomax; limiting the production of cytokines and/or TNF at inflammatory sites, as a consequence of decreasing cell infiltration; for treating diseases and/or congestive heart failure, linked to TNF and IL-1 and for treating pulmonary emphysema or dyspnea associated therewith, emphysema; HIV-1, HIV-2, HIV-3; cytomegalovirus (CMV), adenoviruses, Herpes viruses (Herpes zoster and Herpes simplex), for treating sequelae associated with infection where such infection induces production of detrimental inflammatory cytokines and/or TNF, fungal meningitis, joint tissue damage, hyperplasia, pannus formation and bone resorption, psoriatic arthritis, hepatic failure, bacterial meningitis, Kawasaki syndrome, myocardial infarction, acute liver failure, lyme disease, septic shock, cancer, trauma, and malaria, in a mammal, comprising an amount of a compound according to claim 20 or 21, or a pharmaceutically acceptable salt thereof, that is effective in treating or preventing such disorder or condition and a pharmaceutically acceptable carrier.
- 11. (Currently Amended) A pharmaceutical composition for treating or preventing a disorder or condition that can be treated or prevented by inhibiting chemokine binding to the receptor CCR1

USSN 10/660,052

Page 4 of 29

in a mammal, comprising an amount of a compound according to claim 20-or 21, or a pharmaceutically acceptable salt thereof, effective in treating or preventing such disorder or condition and a pharmaceutically acceptable carrier.

12-19. (Cancelled)

20. (Currently Amended) A compound of the formula

$$(Z)_{e}$$
 $(Y)_{d}$ $(X)_{c}$ $(R^{2})_{b}$ $(R^{1})_{e}$

or the pharmaceutically acceptable salt thereof; wherein

R¹ is <u>independently selected from hydrogen</u>, halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, (C₁-C₆)alkyl, hydroxy or (C₁-C₆)alkylcarbonyloxy;

R² and R³ are each independently selected from (C₁-C₆)alkyl, (C₃-C₈)cycloalkyl, amino(C₁-C₆)alkyl, amino(C₃-C₈)cycloalkyl, (C₁-C₆)alkylamino(C₁-C₆)alkyl, (C₁-C₆)alkylamino(C₃-C₈)cycloalkyl, hydroxy(C₁-C₆)alkyl, (C₁-C₆)alkoxycarbonylamino(C₁-C₆)alkyl, ureido(C₁-C₆)alkyl, (C₁-C₆)alkyl, (C₂-C₉)heteroaryl(C₁-C₆)alkyl or (C₂-C₉)heterocycloalkyl(C₁-C₆)alkyl;

 R^4 is $(R^5)_f(R^6)_g(C_6-C_{10})$ aryl or $(R^5)_f(R^7)_h(C_2-C_9)$ heteroaryl-wherein f, g and h are independently 1 or 2;

 $R^5 \ is \ (C_2-C_9) heterocycloalkylcarbonyl, \ (C_2-C_9) heteroarylcarbonyl, \ (C_2-C_9) heteroaryl(C_1-C_6) alkylaminocarbonyl, \ (C_1-C_6) alkylaminosulfonyl(C_1-C_6) alkylaminocarbonyl, \ (C_1-C_6) alkylaminosulfonyl(C_1-C_6) alkylaminocarbonyl, \ (C_1-C_6) alkylamino(C_1-C_6) alkylamino(C_1-C_6) alkylamino, \ (C_1-C_6) alkylamino(C_1-C_6) alkylamino, \ (C_1-C_6) alkylamino(C_1-C_6) alkylamino, \ (C_1-C_6) alkylamino, \$

USSN 10/660,052

Page 5 of 29

 C_6) alkylcarbonylamino, (C_2 - C_9) heterocycloalkyl(C_1 - C_6) alkylcarbonylamino, aminosulfonyl(C_1 - C_6) and a constant and a consta C₆)alkylcarbonylamino, amino(C₁-C₆)alkylureido, (C₁-C₆)alkylamino(C₁-C₆)alkylureido, ((C₁-C₆)alkylamino(C₁-C₆)alkylureido, C₆)alkyl)₂amino(C₁-C₆)alkylureido, (C₂-C₉)heterocycloalkyl(C₁-C₆)alkylureido, (C₂-C₉)heteroaryl(C₁-C₆)alkylureido, aminosulfonyl(C₁-C₆)alkylureido, aminocarbonyl(C₁- C_6) alkylureido, (C_1-C_6) alkylaminocarbonyl (C_1-C_6) alkylureido, $((C_1-C_6)$ alkyl $)_2$ aminocarbonyl (C_1-C_6) alkyl $)_2$ aminocarbonyl (C_1-C_6) alkyl $)_2$ aminocarbonyl (C_1-C_6) alkyl $)_2$ aminocarbonyl (C_1-C_6) alkyl $)_3$ aminocarbonyl (C_1-C_6) alkyl $)_4$ aminocarbonyl (C_1-C_6) alkyl $)_2$ aminocarbonyl (C_1-C_6) alkyl $)_3$ aminocarbonyl (C_1-C_6) alkyl $)_4$ aminocarbonyl (C_1-C_6) and (C_1-C_6) alkyl $)_4$ aminocarbonyl (C_1-C_6) and C_6) alkylureido, acetylamino (C_1-C_6) alkylureido, (acetyl) $((C_1-C_6)$ alkylureido, acetylamino (C_1-C_6) alkylureido, $amino(C_1-C_6) alkyl sulfonylamino, (C_1-C_6) alkyl sulfonylamino, ((C_1-C_6) alkyl sulfonylamino, ((C_1-C_6) alkyl sulfonylamino), ((C_1-C_6) alkyl sulfonylamino)$ $C_6) alkyl)_2 amino (C_1-C_6) alkyl sulfonylamino, acetylamino (C_1-C_6) alkyl sulfonylamino, (acetyl) ((C_1-C_6) alkyl sulfonylamino), acetylamino (C_1-C_6) alkyl sulfonylamino (C_1-C_6)$ C_6)alkyl)amino(C_1 - C_6)alkylsulfonylamino, ureido(C_1 - C_6)alkylsulfonylamino, (C_1 - $C_6) alkylure ido (C_1-C_6) alkyl sulfonylamino, ((C_1-C_6) alkyl)_2 ure ido (C_1-C_6) alkyl sulfonylamino, (C_1-C_6) alky$ $C_6) alkyl sulfonylamino (C_1-C_6) alkyl sulfonylamino, cyanoguanidino (C_1-C_6) alkyl sulfonylamino, (C_1-C_6) alkyl sulfonylamino (C_1-C_6) alkyl sulfon$ $C_6) alkyl cyanoguanidino (C_1-C_6) alkyl sulfonylamino, ((C_1-C_6) alkyl)_2 cyanoguanidino (C_1-C_6) alkyl sulfonylamino, ((C_1-C_6) alkyl sulfonylamino, ($ C₆)alkylsulfonylamino, aminocarbonyl(C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkoxycarbonylamino(C₁-C₆)alkylsulfonylamino, aminosulfonylamino, (C₁-C₆)alkylaminosulfonylamino, ((C₁-C₆)alkyl)₂aminosulfonylamino, aminocarbonyl(C₁- C_6) alkylamino (C_1 - C_6) alkylsulfonylamino, (C_2 - C_9) heterocycloalkyloxycarbonylamino (C_1 -C₆)alkylsulfonylamino, (C₂-C₉)heteroaryloxycarbonylamino(C₁-C₆)alkylsulfonylamino, cyanoguanidino, (C1-C6)alkylcyanoguanidino, ((C1-C6)alkyl)2cyanoguanidino, (C2-C₉)heterocycloalkylcyanoguanidino, (C₂-C₉)heteroarylcyanoguanidino, (C₂-C₉)heterocycloalkyl(C₁- C_6) alkylcyanoguanidino, (C_2 - C_9) heteroaryl(C_1 - C_6) alkylcyanoguanidino, amino(C_1 - $C_6) alkyl cyanoguanidino, (C_1-C_6) alkyl amino (C_1-C_6) alkyl cyanoguanidino, ((C_1-C_6) alkyl)_2 amino (C_1-C_6) alkyl cyanoguanidino, ((C_1-C_6) alkyl)_2 amino (C_1-C_6) alkyl cyanoguanidino, ((C_1-C_6) alkyl cyanoguanidino,$ C₆)alkylcyanoguanidino, aminocarbonyl(C₁-C₆)alkylcyanoguanidino, (C₁-C₆)alkylaminocarbonyl(C₁-C₆)alkylcyanoguanidino, ((C₁-C₆)alkyl)₂aminocarbonyl(C₁- C_6) alkylcyanoguanidino, aminocarbonyl (C_1 - C_6) alkylamino, (C_1 - C_6) alkylsulfonylamino (C_1 - $C_6) alkylamino, (C_1-C_6) alkoxycarbonylamino (C_1-C_6) alkylamino, aminosulfonyl (C_1-C_6) alkylam$ $(C_2\text{-}C_9) \\ \text{heteroaryl} \\ (C_1\text{-}C_6) \\ \text{alkylamino, acetylamino} \\ (C_1\text{-}C_6) \\ \text{alkylamino, (acetyl)} \\ ((C_1\text{-}C_6)\text{-}C_6) \\$ $C_6) alkyl) amino (C_1-C_6) alkylamino, \ cyano (C_1-C_6) alkylamino alkyl, \ amino carbonyl (C_1-C_6) alkylamino (C_1-C_6) alkylamin$ C_6)alkylamino(C_1 - C_6)alkyl, acetylamino(C_1 - C_6)alkylamino(C_1 - C_6)alkyl, (acetyl)((C_1 - C_6) alkyl) amino (C_1 - C_6) alkylamino (C_1 - C_6) alkyl, (C_1 - C_6) alkoxycarbonylamino (C_1 - C_6) alkylamino (C_1 - C_6) alkyla

USSN 10/660,052

Page 6 of 29

C₆)alkyl, (C₂-C₉)heterocycloalkyloxycarbonylamino(C₁-C₆)alkylamino(C₁-C₆)alkyl, (C₂-C₉)heteroaryloxycarbonylamino(C₁-C₆)alkylamino(C₁-C₆)alkyl, cyanoguanidino(C₁- $C_6) alkylamino (C_1-C_6) alkyl, (C_1-C_6) alkylcyanoguanidino (C_1-C_6) alkylamino (C_1-C_6) alkyl, ((C_1-C_6) alkylcyanoguanidino (C_1-C_6) alkylcyanogu$ C_6) alkylamino (C_1-C_6) alkyl, ureido (C_1-C_6) alkylamino (C_1-C_6) alkylureido (C_1-C_6) C_6)alkylamino(C_1 - C_6)alkyl, ((C_1 - C_6)alkyl)₂ureido(C_1 - C_6)alkylamino(C_1 - C_6)alkyl, $amino carbonyloxy (C_1-C_6) alkylamino (C_1-C_6) alkyl, acetylamino (C_1-C_6) alkylcarbonylamino (C_1$ C_6)alkyl, (acetyl)((C_1 - C_6)alkyl)amino(C_1 - C_6)alkylcarbonylamino(C_1 - C_6)alkyl, aminocarbonyl(C_1 - $C_6) alkyl carbonylamino (C_1-C_6) alkyl, (C_1-C_6) alkylamino carbonyl (C_1-C_6) alkyl carbonylamino (C_1-C_6) alkyl carbon$ $C_6) alkyl, ((C_1-C_6)alkyl)_2 a minosul fonyl (C_1-C_6)alkyl carbonyl a minosul fonyl (C_1-C_6)alkyl)_2 a minosul fonyl (C_1-C_6)alkyl)_3 a minosul fonyl (C_1-C_6)alkyl)_2 a minosul fonyl (C_1-C_6)alkyl)_3 a minosul fonyl (C_1-C_6)alkyl (C_1-C_6)a$ $C_6) alkyl carbonylamino (C_1-C_6) alkyl, (C_2-C_9) heterocycloalkyloxycarbonylamino (C_1-C_9) alkyl, (C_2-C_9) alkyl, (C_2-C_9)$ $cyanoguanidino (C_1-C_6) alkyl carbonylamino (C_1-C_6) alkyl, \ cyano (C_1-C_6) alkyl carbonylamino (C_1-C_6) alkyl carbonyl$ C₆)alkyl, wherein-R⁵ is amino(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₁-C₆)alkylamino(C₁-C₆)alkylaminocarbonyl amino(C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂amino(C₁-C₆) $C_6) alkylamino carbonylamino (C_1-C_6) alkylamino (C_1-C_6) alkylamino carbonylamino (C_1-C_6) alkylamino (C_1-C_6) al$ $C_6) alkyl, (C_1-C_6) alkylcarbonylamino (C_1-C_6) alkylamino carbonylamino (C_1-C_6) alkyl, (C_1-C_6) alkylamino (C_1-C_6) alkylamin$ $C_6) alkyl sulfonylamino (C_1-C_6) alkylamino carbonylamino (C_1-C_6) alkyl, (C_1-C_6) alkoxycarbonylamino (C_1-C_6) alkylamino (C_1$ $amino(C_1-C_6) alkylamino carbonylamino (C_1-C_6) alkyl, (C_2-C_9) heterocycloalkyloxycarbonylamino (C_1-C_6) alkylamino (C_1-C_6) al$ $amino(C_1-C_6) alkylamino carbonylamino (C_1-C_6) alkyl, (C_2-C_9) heteroaryloxy carbonylamino (C_1-C_6) alkylamino (C_1-C_6) alkylam$ C_6) alkylaminocarbonylamino (C_1 - C_6) alkyl, (C_2 - C_9) heterocycloalkyl (C_1 - C_6) alkylaminocarbonyl $amino(C_1-C_6) alkyl, (C_2-C_9) heteroaryl (C_1-C_6) alkylamino carbonylamino (C_1-C_6) alkyl, ureido (C_1-C_6) alkylamino (C_1-C_6)$ $C_6) alkylure ido(C_1-C_6) alkyl, (C_1-C_6) alkylure ido(C_1-C_6) alkylure ido(C_1-C_6) alkyl, ((C_1-C_6) alkylure ido(C_1-C_6) al$ C_6)alkyl)₂ureido(C_1 - C_6)alkylureido(C_1 - C_6)alkyl, excyanoguanidino(C_1 - C_6)alkylureido(C_1 - C_6)alkyl, $amino(C_1-C_6) alkylsul fonylamino(C_1-C_6) alkyl, (C_1-C_6) alkylamino(C_1-C_6) alkylsul fonylamino(C_1-C_6) alkylsul fonylamino($ $C_6) alkyl, ((C_1-C_6)alkyl)_2 amino (C_1-C_6)alkyl sulfonylamino (C_1-C_6)alkyl, acetylamino (C_1-C_6)alkyl)_2 amino (C_1-C_6)alkyl sulfonylamino (C_1-C_6)alkyl)_2 amino (C_1-C_6)alkyl sulfonylamino (C_1-C_6)alkyl su$ $C_6) alkyl sulfonylamino (C_1-C_6) alkyl, (acetyl) ((C_1-C_6) alkyl) amino (C_1-C_6) alkyl sulfonylamino (C_1-C_6) alkyl sul$ C₆)alkyl, ureido(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, (C₁-C₆)alkylureido(C₁- $C_6) alkyl sulfonylamino (C_1-C_6) alkyl, ((C_1-C_6)alkyl)_2 ure ido (C_1-C_6) alkyl sulfonylamino (C_1-C_6) alkyl sulfonylamino$ $(C_1\text{-}C_6) alkyl sulfonylamino (C_1\text{-}C_6) alkyl sulfonylamino (C_1\text{-}C_6) alkyl, \ cyanoguanidino (C_1\text{-}C_6) alkyl sulfonylamino (C_1\text{-}C_6) alkyl sulfonyl$

USSN 10/660,052

Page 7 of 29

 $C_6) alkyl sulfonylamino (C_1-C_6) alkyl, (C_1-C_6) alkyl (cyanoguanidino) (C_1-C_6) alkyl sulfonylamino (C_1-C_6) alkyl sul$ C_6)alkyl, $((C_1-C_6)alkyl)_2$ (cyanoguanidino) $(C_1-C_6)alkyl$ sulfonylamino $(C_1-C_6)alkyl$, $amino carbonyl (C_1-C_6) alkyl sulfonylamino (C_1-C_6) alkyl, (C_1-C_6) alkoxy carbonylamino (C_1-C_6) alkyl sulfonylamino ($ $\label{eq:condition} C_6) alkyl sulfonylamino (C_1-C_6) alkyl, (C_2-C_9) heterocycloalkyloxycarbonylamino (C_1-C_6) alkyl sulfonylamino (C_1-C_6) alkyl su$ C_6) alkylsul fonylamino (C_1 - C_6) alkyl, (C_2 - C_9) heteroaryloxy carbonylamino (C_1 - C_6)alkylsulfonylamino(C_1 - C_6)alkyl, aminosulfonylamino(C_1 - C_6)alkyl, (C_1 - C_6)alkylaminosulfonylamino(C_1 - C_6)alkyl, ((C_1 - C_6)alkyl)₂aminosulfonylamino(C_1 - C_6)alkyl, $cyanoguanidino(C_1-C_6)alkyl, (C_1-C_6)alkyl(cyanoguanidino)(C_1-C_6)alkyl, ((C_1-C_6)alkyl, ((C_1-C_6)alk$ C_6)alkyl)₂(cyanoguanidino)(C_1 - C_6)alkyl, (C_2 - C_9)heterocycloalkyl(cyanoguanidino)(C_1 - C_6)alkyl, (C2-C9)heteroaryl(cyanoguanidino)(C1-C6)alkyl, (C2-C9)heterocycloalkyl(C1- C_6)alkyl(cyanoguanidino)(C_1 - C_6)alkyl, (C_2 - C_9)heteroaryl(C_1 - C_6)alkyl(cyanoguanidino)(C_1 -C₆)alkyl, amino(C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl, (C₁-C₆)alkylamino(C₁-C6)alkyl(cyanoguanidino)(C1-C6)alkyl, ((C1-C6)alkyl)2amino(C1-C6)alkyl(cyanoguanidino)(C1-C6)alkyl C_6)alkyl, aminocarbonyl(C_1 - C_6)alkyl(cyanoguanidino)(C_1 - C_6)alkyl, (C_1 - C_6)alkylaminocarbonyl(C_1 -C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂aminocarbonyl(C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl, wherein R⁵ is (C₂-C₉)heterocycloalkylsulfonyl, amino(C₁- $C_6) alkylaminosulfonyl, (C_1-C_6) alkylamino (C_1-C_6) alkylaminosulfonyl, ((C_1-C_6) alkyl)_2 amino (C_1-C_6) alkylaminosulfonyl, (C_1-C_6) alkylaminosulfonyl, ((C_1-C_6) alkylaminos$ C_6) alkylaminosulfonyl, (C_2-C_9) heteroarylaminosulfonyl, ureido (C_1-C_6) alkylaminosulfonyl, (C_1-C_6) $C_6) alkylure ido (C_1-C_6) alkylaminosul fonyl, ((C_1-C_6) alkyl)_2 ure ido (C_1-C_6) alkylaminosul fonyl, (C_1-C_6) alky$ C_6) alkylsul fonylamino (C_1 - C_6) alkylamino sulfonyl, (C_1 - C_6) alkoxycarbonylamino (C_1 -C₆)alkylaminosulfonyl, (C₂-C₉)heterocycloalkyloxycarbonylamino(C₁-C₆)alkylaminosulfonyl, (C₂-C₉)heteroaryloxycarbonylamino(C₁-C₆)alkylaminosulfonyl, aminocarbonyl(C₁- C_6) alkylaminosulfonyl, cyanoguanidino (C_1 - C_6) alkylaminosulfonyl, (C_2 - C_9) heteroaryl (C_1 - C_6) alkylaminosulfonyl, (C_2 - C_9) heteroaryl (C_1 - C_6) alkylaminosulfonyl, (C_2 - C_9) heteroaryl (C_1 - C_6) alkylaminosulfonyl, (C_2 - C_9) heteroaryl (C_1 - C_6) alkylaminosulfonyl, (C_2 - C_9) heteroaryl (C_1 - C_6) alkylaminosulfonyl, (C_2 - C_9) heteroaryl (C_1 - C_6) alkylaminosulfonyl, (C_2 - C_9) heteroaryl (C_1 - C_6) alkylaminosulfonyl, (C_2 - C_9) heteroaryl (C_1 - C_9) alkylaminosulfonyl, (C_2 - C_9) heteroaryl (C_1 - C_9) alkylaminosulfonyl, (C_2 - C_9) heteroaryl (C_1 - C_9) C₆)alkylaminosulfonyl, (C₂-C₉)heterocycloalkylaminosulfonyl, halo(C₁-C₆)alkylaminocarbonyl, $\label{eq:convergence} \mbox{hydroxy}(C_1\text{-}C_6) alkylure ido, halo(C_1\text{-}C_6) alkylure i$ $C_6) alkylamino (C_1-C_6) alkyl, \ hydroxy (C_1-C_6) alkylamino carbonylamino (C_1-C_6) alkyl, \ halo (C_1-C_6) alkylamino (C_1-C_6)$ C_6)alkylsulfonylamino(C_1 - C_6)alkyl, aminosulfonyl, (C_1 - C_6)alkylaminosulfonyl, ((C_1 - C_6)alkylsulfonylaminosulfonyl, ((C_1 - C_6)alkylsulfonylaminos $\label{eq:condition} C_6) alkyl)_2 a minosulfonyl, \ hydroxy (C_1-C_6) alkylaminosulfonyl, \ or \ (C_1-C_6) alkoxy (C_1-C_6) alkyl)_2 a minosulfonyl, \ hydroxy (C_1-C_6) alkyl)_3 a minosulfonyl, \ hydroxy (C_1-C_6) alkyl)_4 a minosulfonyl, \ hydroxy (C_1-C_6) alkylaminosulfonyl, \ or \ (C_1-C_6) alkyl)_4 a minosulfonyl, \ hydroxy (C_1-C_6) alkylaminosulfonyl, \$ C₆)alkylaminosulfonyl;

USSN 10/660,052

Page 8 of 29

R⁶ and R⁷ are each independently halo, halo(C₁-C₆)alkyl, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, trifluoromethyl, trifluoromethoxy, hydroxy, aminocarbonyl, cyano, ureido, (C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkoxycarbonylamino or glycinamino;

a is 1, 2, 3, 4 or 5;

b is 0, 1, 2, 3 or 4;

c is 1;

d is 1:

e is 1:

j is 1, 2, 3, or 4;

Y is CH₂;

X is C(O); and

Z is oxygen.

21. (Withdrawn) A compound of the formula

$$(Z)_{e}$$
 $(Y)_{d}$ $(X)_{c}$ $(R^{2})_{b}$ $(R^{1})_{e}$

or the pharmaceutically acceptable salt thereof; wherein

 R^1 is hydrogen, halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, (C_1 - C_6)alkyl, hydroxy or (C_1 - C_6)alkylcarbonyloxy;

 R^2 and R^3 are each independently selected from (C_1-C_6) alkyl, (C_3-C_8) cycloalkyl, amino (C_1-C_6) alkyl, amino (C_3-C_8) cycloalkyl, (C_1-C_6) alkylamino (C_1-C_6) alkyl, (C_1-C_6) alkyl, (C_1-C_6) alkyl, (C_1-C_6) alkyl, (C_1-C_6) alkyl, ureido (C_1-C_6) alkyl, (C_1-C_6) alkyl, (C_1-C_6) alkyl, (C_2-C_9) heteroaryl (C_1-C_6) alkyl or (C_2-C_9) heterocycloalkyl (C_1-C_6) alkyl;

 R^4 is $(R^5)_f(R^6)_g(C_6-C_{10})$ aryl or $(R^5)_f(R^7)_h(C_2-C_9)$ heteroaryl wherein f, g and h are independently 1 or 2;

 $R^5 \ is \ (C_2-C_9) heterocycloalkylcarbonyl, \ (C_2-C_9) heteroarylcarbonyl, \ (C_2-C_9) heteroaryl \ (C_1-C_9) heteroarylcarbonyl, \ (C_2-C_9) heteroaryl$

USSN 10/660,052

Page 9 of 29

C₆)alkylaminocarbonyl, (C₂-C₉)heterocycloalkyl(C₁-C₆)alkylaminocarbonyl, (C₁-C₆)alkylsulfonylamino(C₁-C₆)alkylaminocarbonyl, ureido(C₁-C₆)alkylaminocarbonyl, (C₁-C₆)alkylureido(C₁-C₆)alkylaminocarbonyl, ((C₁-C₆)alkyl)₂ureido(C₁-C₆)alkylaminocarbonyl, $aminosulfonyl (C_1-C_6) alkylaminocarbonyl, (C_1-C_6) alkylaminosulfonyl (C_1-C_6) alkylaminocarbonyl, (C_1-C_6) alkylaminoc$ $(C_1-C_6) alkyl sulfonylamino (C_1-C_6) alkyl carbonylamino, cyanoguanidino (C_1-C_6) alkyl carbonylamino (C_1-C_6) alky$ (C1-C6)alkylcyanoguanidino(C1-C6)alkylcarbonylamino, ((C1-C6)alkyl)2cyanoguanidino(C1-C₆)alkylcarbonylamino, aminocarbonyl(C₁-C₆)alkylcarbonylamino, (C₂-C₉)heteroaryl(C₁- C_6) alkylcarbonylamino, (C_2 - C_9) heterocycloalkyl(C_1 - C_6) alkylcarbonylamino, aminosulfonyl(C_1 -C₆)alkylcarbonylamino, amino(C₁-C₆)alkylureido, (C₁-C₆)alkylamino(C₁-C₆)alkylureido, ((C₁-C₆)alkylureido, C₆)alkyl)₂amino(C₁-C₆)alkylureido, (C₂-C₉)heterocycloalkyl(C₁-C₆)alkylureido, (C₂- C_9)heteroaryl(C_1 - C_6)alkylureido, aminosulfonyl(C_1 - C_6)alkylureido, aminocarbonyl(C_1 - C_6) alkylureido, (C_1-C_6) alkylaminocarbonyl (C_1-C_6) alkylureido, $((C_1-C_6)$ alkyl $)_2$ aminocarbonyl (C_1-C_6) alkyl $)_3$ aminocarbonyl (C_1-C_6) alkyl $)_4$ aminocarbonyl (C_1-C_6) alkyl $)_2$ aminocarbonyl (C_1-C_6) alkyl $)_3$ aminocarbonyl (C_1-C_6) alkyl $)_4$ aminocarbonyl (C_1-C_6) and (C_1-C_6) alkyl $)_4$ aminocarbonyl (C_1-C_6) and (C_1-C_6) alkyl $)_4$ aminocarbonyl (C_1-C_6) and (C_1-C_6) C_6) alkylureido, acetylamino (C_1 - C_6) alkylureido, (acetyl) ((C_1 - C_6) alkylureido, acetylamino (C_1 - C_6) alkylureido, acetyl amino(C1-C6)alkylsulfonylamino, (C1-C6)alkylamino(C1-C6)alkylsulfonylamino, ((C1-C6)alkylsulfonylamino, ((C1-C6)alkylsulfonylamino) $C_6) alkyl)_2 amino (C_1-C_6) alkyl sulfonylamino, acetylamino (C_1-C_6) alkyl sulfonylamino, (acetyl) ((C_1-C_6) alkyl sulfonylamino), acetylamino (C_1-C_6) alkyl sulfonylamino (C_1-C_6)$ C_6) alkyl) amino (C_1 - C_6) alkylsulfonylamino, ureido (C_1 - C_6) alkylsulfonylamino, (C_1 - $C_6) alkylure ido (C_1-C_6) alkylsul fonylamino, ((C_1-C_6) alkyl)_2 ure ido (C_1-C_6) alkylsul fonylamino, (C_1-C_6) alkylsul fonylamino, (C_1-C_6) alkylsul fonylamino, ((C_1-C_6) alkylsu$ $C_6) alkyl sulfonylamino (C_1-C_6) alkyl sulfonylamino, cyanoguanidino (C_1-C_6) alkyl sulfonylamino, (C_1-C_6) alkyl sulf$ C6)alkylcyanoguanidino(C1-C6)alkylsulfonylamino, ((C1-C6)alkyl)2cyanoguanidino(C1-C₆)alkylsulfonylamino, aminocarbonyl(C₁-C₆)alkylsulfonylamino, (C₁- C_6) alkoxycarbonylamino (C_1 - C_6) alkylsulfonylamino, aminosulfonylamino, (C_1 - C_6) alkylaminosul fonylamino, ((C_1 - C_6) alkyl) 2 aminosul fonylamino, aminocarbonyl (C_1 - $C_6) alkylamino (C_1-C_6) alkylsul fonylamino, (C_2-C_9) heterocycloalkyloxycarbonylamino (C_1-C_6) alkylamino ($ C_6) alkylsul fonylamino, (C_2-C_9) heteroaryloxy carbonylamino (C_1-C_6) alkylsul fonylamino, cyanoguanidino, (C1-C6)alkylcyanoguanidino, ((C1-C6)alkyl)2cyanoguanidino, (C2- $\label{eq:constraint} C_9) heterocycloalkyl (C_2-C_9) heteroaryl cyanoguanidino, (C_2-C_9) heterocycloalkyl (C_1-C_9) heterocyc$ C_6) alkylcyanoguanidino, (C_2-C_9) heteroaryl (C_1-C_6) alkylcyanoguanidino, amino (C_1-C_6) alkylcyanoguanidino, amino (C_1-C_6) $C_6) alkyl cyanoguanidino, (C_1-C_6) alkyl amino (C_1-C_6) alkyl cyanoguanidino, ((C_1-C_6) alkyl)_2 amino (C_1-C_6) alkyl cyanoguanidino, ((C_1-C_6) alkyl cyanoguanidino), ($ C₆)alkylcyanoguanidino, aminocarbonyl(C₁-C₆)alkylcyanoguanidino, (C₁-

USSN 10/660,052

Page 10 of 29

C₆)alkylaminocarbonyl(C₁-C₆)alkylcyanoguanidino, ((C₁-C₆)alkyl)₂aminocarbonyl(C₁-C₆)alkylcyanoguanidino, aminocarbonyl(C₁-C₆)alkylamino, (C₁-C₆)alkylsulfonylamino(C₁- C_6) alkylamino, (C_1-C_6) alkoxycarbonylamino (C_1-C_6) alkylamino, aminosulfonyl (C_1-C_6) alkylamino, (C_2-C_9) heteroaryl (C_1-C_6) alkylamino, acetylamino (C_1-C_6) alkylamino, (acetyl) $((C_1-C_6)$ alkylamino) $\label{eq:constraint} C_6) alkyl amino (C_1-C_6) alkyl amino (C_$ C₆)alkylamino(C₁-C₆)alkyl, acetylamino(C₁-C₆)alkylamino(C₁-C₆)alkyl, (acetyl)((C₁- $C_6) alkyl) amino (C_1-C_6) alkylamino (C_1-C_6) alkyl, (C_1-C_6) alkoxycarbonylamino (C_1-C_6) alkylamino (C_1 C_6$)alkyl, (C_2-C_9) heterocycloalkyloxycarbonylamino (C_1-C_6) alkylamino (C_1-C_6) alkyl, (C_2-C_9) C_9)heteroaryloxycarbonylamino(C_1 - C_6)alkylamino(C_1 - C_6)alkyl, cyanoguanidino(C_1 - $C_6) alkylamino (C_1-C_6) alkyl, (C_1-C_6) alkylcyanoguanidino (C_1-C_6) alkylamino (C_1-C_6) alkyl, ((C_1-C_6) alkylcyanoguanidino (C_1-C_6) alkylcyanogu$ $C_6) alkyl)_2 cyanoguanidino (C_1-C_6) alkylamino (C_1-C_6) alkyl, (C_1-C_6) alkylsulfonylamino (C_1-$ C₆)alkylamino(C₁-C₆)alkyl, ureido(C₁-C₆)alkylamino(C₁-C₆)alkyl, (C₁-C₆)alkylureido(C₁-C₆)alkylamino(C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂ureido(C₁-C₆)alkylamino(C₁-C₆)alkyl, $amino carbonyloxy (C_1-C_6) alkylamino (C_1-C_6) alkyl, acetylamino (C_1-C_6) alkylcarbonylamino (C_1$ $C_6) alkyl, (acetyl) ((C_1-C_6)alkyl) amino (C_1-C_6)alkyl carbonyl amino (C_1-C_6)alkyl, amino carbonyl (C_1-C_6)alkyl) amino (C_$ C_6) alkylcarbonylamino (C_1 - C_6) alkyl, (C_1 - C_6) alkylamino carbonyl (C_1 - C_6) alkylcarbonylamino (C_1 - C_6) alk C_6)alkyl, $((C_1-C_6)alkyl)_2$ aminocarbonyl (C_1-C_6) alkylcarbonylamino (C_1-C_6) alkyl, aminosulfonyl (C_1-C_6) alkyl, C_6)alkylcarbonylamino(C_1 - C_6)alkyl, (C_2 - C_9)heterocycloalkyloxycarbonylamino(C_1 - C_6)alkyl, cyanoguanidino(C₁-C₆)alkylcarbonylamino(C₁-C₆)alkyl, cyano(C₁-C₆)alkylcarbonylamino(C₁-C₆)alkyl, wherein R⁵ is amino(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₁- C_6)alkylamino (C_1-C_6) alkylaminocarbonyl amino (C_1-C_6) alkyl, $((C_1-C_6)$ alkyl)₂amino (C_1-C_6) alkyl $C_6) alkylamino carbonylamino (C_1-C_6) alkyl, amino carbonyl (C_1-C_6) alkylamino carbonylamino (C_1-C_6) alkylamino (C_1-C_6$ $C_6) alkyl, (C_1-C_6) alkyl carbonylamino (C_1-C_6) alkylamino carbonylamino (C_1-C_6) alkyl, (C_1-C_6) alkylamino (C_1-C_6) alkylami$ $C_6) alkyl sulfonylamino (C_1-C_6) alkylamino carbonylamino (C_1-C_6) alkyl, (C_1-C_6) alkoxycarbonylamino (C_1-C_6) alkylamino (C_1$ amino(C1-C6)alkylaminocarbonylamino(C1-C6)alkyl, (C2-C9)heterocycloalkyloxycarbonyl amino(C1-C6)alkylaminocarbonylamino(C1-C6)alkyl, (C2-C9)heteroaryloxycarbonylamino(C1- C_6)alkylaminocarbonylamino (C_1-C_6) alkyl, (C_2-C_9) heterocycloalkyl (C_1-C_6) alkylaminocarbony $lamino(C_1-C_6) alkyl, (C_2-C_9) heteroaryl (C_1-C_6) alkylamino carbonylamino (C_1-C_6) alkyl, ureido (C_1-C_6) alkylamino (C_1-C_6)$ $C_6) alkylure ido(C_1-C_6) alkyl, (C_1-C_6) alkylure ido(C_1-C_6) alkylure ido(C_1-C_6$

USSN 10/660,052 Page 11 of 29 Amendment and Response to OA dated June 25, 2004

C₆)alkyl)₂ureido(C₁-C₆)alkylureido(C₁-C₆)alkyl or cyanoguanidino(C₁-C₆)alkylureido(C₁-C₆)alkyl, $amino(C_1-C_6) alkylsulfonylamino(C_1-C_6) alkyl, (C_1-C_6) alkylamino(C_1-C_6) alkylsulfonylamino(C_1-C_6) alky$ C_6)alkyl, ((C_1 - C_6)alkyl)₂amino(C_1 - C_6)alkylsulfonylamino(C_1 - C_6)alkyl, acetylamino(C_1 - $C_6) alkyl sulfonylamino (C_1-C_6) alkyl, (acetyl) ((C_1-C_6) alkyl) amino (C_1-C_6) alkyl sulfonylamino (C_1-C_6) alkyl sul$ C_6) alkyl, ureido (C_1 - C_6) alkylsulfonylamino (C_1 - C_6) alkyl, (C_1 - C_6) alkylureido (C_1 - $C_6) alkyl sulfonylarnino (C_1-C_6) alkyl, ((C_1-C_6) alkyl)_2 ureido (C_1-C_6) alkyl sulfonylarnino (C_1-C_6) alkyl sulfonylarnino$ (C_1-C_6) alkylsulfonylamino (C_1-C_6) alkylsulfonylamino (C_1-C_6) alkyl, cyanoguanidino (C_1-C_6) alkylsulfonylamino (C_1-C_6) a C_6) alkylsul fonylamino (C_1 - C_6) alkyl, (C_1 - C_6) alkyl (cyanoguanidino) (C_1 - C_6) alkylsul fonylamino (C_1 - C_6) alkylsul C_6)alkyl, $((C_1-C_6)alkyl)_2$ (cyanoguanidino) $(C_1-C_6)alkyl$ sulfonylamino $(C_1-C_6)alkyl$, $amino carbonyl (C_1-C_6) alkyl sulfonylamino (C_1-C_6) alkyl, (C_1-C_6) alkoxycarbonylamino (C_1-C_6) alkyl sulfonylamino (C$ $C_6) alkyl sulfonylamino (C_1-C_6) alkyl, (C_2-C_9) heterocycloalkyloxycarbonylamino (C_1-C_6) alkyl sulfonylamino (C_1-C_6)$ C₆)alkylsulfonylamino(C₁-C₆)alkyl, (C₂-C₉)heteroaryloxycarbonylamino(C₁- $C_6) alkyl sulfonylamino (C_1-C_6) alkyl, \ aminosulfonylamino (C_1-C_6) alkyl, \ (C_1-C_6) alkyl sulfonylamino (C_1-C_6) al$ $C_6) alkylaminosulfonylamino (C_1-C_6) alkyl, ((C_1-C_6)alkyl)_2 aminosulfonylamino (C_1-C_6) alkyl, ((C_1-C_6)alkyl)_2 aminosulfonylamino (C_1-C_6) alkyl, ((C_1-C_6)alkyl)_3 aminosulfonylamino (C_1-C_6) alkyl, ((C_1-C_6)alkyl)_4 aminosulfonylamino (C_1-C_6) alkyl, ((C_1-C_6)alkyl)_5 aminosulfonylamino (C_1-C_6) alkyl, ((C_1-C_6)alkyl)_6 aminosulfonylamino (C_1-C_6) alkyl, ((C_1-C_6)alkyl)_7 aminosulfonylamino (C_1-C_6) alkyl, ((C_1-C_6)alkyl)_7$ cyanoguanidino(C₁-C₆)alkyl, (C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl, ((C₁- C_6)alkyl)₂(cyanoguanidino)(C_1 - C_6)alkyl, (C_2 - C_9)heterocycloalkyl(cyanoguanidino)(C_1 - C_6)alkyl, $(C_2\text{-}C_9) heteroaryl (cyanoguanidino) (C_1\text{-}C_6) alkyl, (C_2\text{-}C_9) heterocycloalkyl (C_1\text{-}C_9) heterocycloalkyl (C_1\text{-}C_9)$ C_6) alkyl (cyanoguanidino) (C_1 - C_6) alkyl, (C_2 - C_9) heteroaryl (C_1 - C_6) alkyl (cyanoguanidino) (C_1 - C_1 - C_2) alkyl (cyanoguanidino) C_6)alkyl, amino(C_1 - C_6)alkyl(cyanoguanidino)(C_1 - C_6)alkyl, (C_1 - C_6)alkylamino(C_1 -C6)alkyl(cyanoguanidino)(C1-C6)alkyl, ((C1-C6)alkyl)2amino(C1-C6)alkyl(cyanoguanidino)(C1-C6)alkyl C₆)alkyl, aminocarbonyl(C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl, (C₁-C₆)alkylaminocarbonyl(C₁- $C_6) alkyl (cyanoguanidino) (C_1-C_6) alkyl, ((C_1-C_6) alkyl)_2 aminocarbonyl (C_1-C_6) alkyl)_2 aminocarbonyl (C_1-C_6) alkyl)_3 aminocarbonyl (C_1-C_6) alkyl)_2 aminocarbonyl (C_1-C_6) alkyl)_3 aminocarbonyl (C_1-C_6) alkyl)_3 aminocarbonyl (C_1-C_6) alkyl)_4 aminocarbonyl (C_1-C_6) alkyl)_5 aminocarbonyl (C_1-C_6) alkyl)_6 aminocarbonyl (C_1-C_6) alkyl)_7 aminocarbonyl (C_1-C_6) alkyl)_8 aminocarbonyl (C_1-C_6) alkyl)_9 aminocarbonyl (C_1-C_6) alkyl (C_1-C_$ C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl, wherein R⁵ is (C₂-C₉)heterocycloalkylsulfonyl, amino(C₁-C₆)alkyl $\label{eq:continuous} C_6) alkylaminosulfonyl, (C_1-C_6) alkylaminosulfonyl, ((C_1-C_6) alkyl)_2 amino (C_1-C_6) alkylaminosulfonyl, ((C_1-C_6) alkylamin$ $C_6) alkylaminosulfonyl, (C_2-C_9) heteroary laminosulfonyl, ureido (C_1-C_6) alkylaminosulfonyl, (C_1-C_6) alkylaminosulfonyl, (C_2-C_9) heteroary laminosulfonyl, ureido (C_1-C_6) alkylaminosulfonyl, (C_1-C_9) heteroary laminosulfonyl, (C_1-C_9) heteroary laminosulfony$ $C_6) alkylure ido (C_1-C_6) alkylaminosul fonyl, ((C_1-C_6) alkyl)_2 ure ido (C_1-C_6) alkylaminosul fonyl, (C_1-C_6) alky$ $C_6) alkyl sulfonylamino (C_1-C_6) alkylamino sulfonyl, (C_1-C_6) alkoxycarbonylamino (C_1-C_6) alkylsulfonylamino (C_1-C_6) alkyl$ C_6) alkylaminosulfonyl, (C_2-C_9) heterocycloalkyloxycarbonylamino (C_1-C_6) alkylaminosulfonyl, (C_2-C_9) C_9) heteroaryloxy carbonylamino (C_1 - C_6) alkylamino sulfonyl, amino carbonyl (C_1 -

USSN 10/660,052

Page 12 of 29

 $C_6) alkylaminosulfonyl, cyanoguanidino(C_1-C_6) alkylaminosulfonyl, (C_2-C_9) heteroaryl(C_1-C_6) alkylaminosulfonyl, (C_2-C_9) heterocycloalkylaminosulfonyl, halo(C_1-C_6) alkylaminocarbonyl, hydroxy(C_1-C_6) alkylamino(C_1-C_6) alkylsulfonylamino, (C_1-C_6) alkoxycarbonyl(C_1-C_6) alkylamino(C_1-C_6) alkylaminocarbonylamino(C_1-C_6) alkyl, halo(C_1-C_6) alkylsulfonylamino(C_1-C_6) alkyl, aminosulfonyl, (C_1-C_6) alkylaminosulfonyl, ((C_1-C_6) alkylaminosulfonyl, hydroxy(C_1-C_6) alkylaminosulfonyl, or (C_1-C_6) alkoxy(C_1-C_6) alkylaminosulfonyl;$

R⁶ and R⁷ are each independently halo, halo(C₁-C₆)alkyl, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, trifluoromethyl, trifluoromethoxy, hydroxy, aminocarbonyl, cyano, ureido, (C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkoxycarbonylamino or glycinamino;

```
a is 1, 2, 3, 4 or 5;
b is 0, 1, 2, 3 or 4;
c is 1;
d is 1;
e is 1;
j is 1, 2, 3, or 4;
Y is CH<sub>2</sub>;
X is C(O); and
Z is NR<sup>9</sup> wherein R<sup>9</sup> is hydrogen or (C<sub>1</sub>-C<sub>6</sub>)alkyl.
```

- 22. (Currently Amended) The compound of claim 20 er 21-wherein R^5 is (C_2 - C_9)heterocycloalkylcarbonyl, (C_2 - C_9)heteroarylcarbonyl, (C_2 - C_9)heteroarylcarbonyl, (C_2 - C_9)heterocycloalkyl(C_1 - C_6)alkylaminocarbonyl, (C_1 - C_6)alkylaminocarbonyl, ureido(C_1 - C_6)alkylaminocarbonyl, (C_1 - C_6)alkylaminocarbonyl, ureido(C_1 - C_6)alkylaminocarbonyl, aminosulfonyl(C_1 - C_6)alkylaminocarbonyl or (C_1 - C_6)alkylaminocarbonyl.
- 23. (Currently Amended) The compound of claim 20 or 21-wherein R⁵ is (C₁-C₆)alkylsulfonylamino(C₁-C₆)alkylcarbonylamino, cyanoguanidino(C₁-C₆)alkylcarbonylamino, (C₁-C₆)alkylcarbonylamino, (C₁-C₆

USSN 10/660,052 Page 13 of 29 Amendment and Response to OA dated June 25, 2004

 C_6)alkylcyanoguanidino(C_1 - C_6)alkylcarbonylamino, ((C_1 - C_6)alkylcarbonylamino, aminocarbonyl(C_1 - C_6)alkylcarbonylamino, (C_2 - C_9)heterocycloalkyl(C_1 - C_6)alkylcarbonylamino, or aminosulfonyl(C_1 - C_6)alkylcarbonylamino.

- 24. (Currently Amended) The compound of claim 20 or 21-wherein R^5 is amino(C_1 - C_6)alkylureido, (C_2 - C_9)heterocycloalkyl(C_1 - C_6)alkylureido, (C_2 - C_9)heteroaryl(C_1 - C_6)alkylureido, aminocarbonyl(C_1 - C_6)alkylureido, (C_1 - C_6)alkylureido, aminocarbonyl(C_1 - C_6)alkylureido, acetylamino(C_1 - C_6)alkylureido, or (acetyl)((C_1 - C_6)alkylureido.
- 25. (Currently Amended) The compound of claim 20 er-21-wherein R⁵ is amino(C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkylsulfonylamino, ((C₁-C₆)alkyl)₂amino(C₁-C₆)alkylsulfonylamino, ((C₁-C₆)alkyl)₂amino(C₁-C₆)alkylsulfonylamino, acetylamino(C₁-C₆)alkylsulfonylamino, (acetyl)(((C₁-C₆)alkyl)amino(C₁-C₆)alkylsulfonylamino, ureido(C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkylsulfonylamino, ((C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkylsulfonylamino, cyanoguanidino(C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkylsulfonylamino, aminocarbonyl(C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkylsulfonylamino, aminocarbonyl(C₁-C₆)alkylsulfonylamino, aminocarbonyl(C₁-C₆)alkylsulfonylamino, aminocarbonyl(C₁-C₆)alkylsulfonylamino, (C₂-C₉)heterocycloalkyloxycarbonylamino(C₁-C₆)alkylsulfonylamino or (C₂-C₉)heterocycloalkyloxycarbonylamino(C₁-C₆)alkylsulfonylamino.

USSN 10/660,052

Page 14 of 29

 $C_6) alkylamino(C_1-C_6) alkylcyanoguanidino, ((C_1-C_6)alkyl)_2 amino(C_1-C_6) alkylcyanoguanidino, aminocarbonyl(C_1-C_6) alkylcyanoguanidino, (C_1-C_6) alkylaminocarbonyl(C_1-C_6) alkylcyanoguanidino or ((C_1-C_6)alkyl)_2 aminocarbonyl(C_1-C_6) alkylcyanoguanidino_<math>\frac{1}{2}$ wherein R^5 is aminocarbonyl(C_1-C_6) alkylamino, (C_1-C_6) alkylamino(C_1-C_6) alkylamino, (C_1-C_6) alkylamino, (C_2-C_6) alkylamino(C_1-C_6) alkylamino, acetylamino(C_1-C_6) alkylamino or (acetyl)((C_1-C_6) alkylamino(C_1-C_6) alkylamino). (C_6) alkylamino. (C_6) alkylamino. (C_6) alkylamino)

- 27. (Currently Amended) The compound of claim 20 or 21 wherein R⁵ is cyano(C₁-C₆)alkylaminoalkyl or aminocarbonyl(C₁-C₆)alkylamino(C₁-C₆)alkyl.
- 28. (Currently Amended) The compound of claim 20 or 21-wherein R⁵ is acetylamino(C₁-C₆)alkylamino(C₁-C₆)alkyl, (acetyl)((C₁-C₆)alkyl)amino(C₁-C₆)alkylamino(C₁-C₆)alkyl, (C₁-C₆)alkylamino(C₁-C₆)alkylamino(C₁-C₆)alkyl, (C₂-C₉)heterocycloalkyloxycarbonylamino(C₁-C₆)alkylamino(C₁-C₆)alkyl, cyanoguanidino(C₁-C₆)alkylamino(C₁-C₆)alkylamino(C₁-C₆)alkylamino(C₁-C₆)alkylamino(C₁-C₆)alkylamino(C₁-C₆)alkylamino(C₁-C₆)alkyl₂cyanoguanidino(C₁-C₆)alkylamino(C₁-C₆)alkyl₃, (C₁-C₆)alkyl₃, (C₁-C₆)alkyl₃, (C₁-C₆)alkyl₃, (C₁-C₆)alkyl₄, (C₁-C₆)alkyl₄, (C₁-C₆)alkyl₆, (C₁-C
- 29. (Currently Amended) The compound of claim 20 or 21-wherein R⁵ is acetylamino(C₁-C₆)alkylcarbonylamino(C₁-C₆)alkyl, (acetyl)((C₁-C₆)alkyl)amino(C₁-C₆)alkylcarbonylamino(C₁-C₆)alkyl, aminocarbonyl(C₁-C₆)alkylcarbonylamino(C₁-C₆)alkylcarbonylamino(C₁-C₆)alkylcarbonylamino(C₁-C₆)alkylcarbonylamino(C₁-C₆)alkyl, aminosulfonyl(C₁-C₆)alkylcarbonylamino(C₁-C₆)alkyl, (C₂-C₉)heterocycloalkyloxycarbonylamino(C₁-C₆)alkyl, cyanoguanidino(C₁-C₆)alkylcarbonylamino(C₁-C₆)alkyl or cyano(C₁-C₆)alkylcarbonylamino(C₁-C₆)alkyl.

USSN 10/660,052 Page 15 of 29 Amendment and Response to OA dated June 25, 2004

- 30. (Currently Amended) The compound of claim 20 or 21-wherein R⁵ is amino(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₁-C₆)alkylamino(C₁-C₆)alkylaminocarbonyl amino(C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂amino(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, aminocarbonyl(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₁-C₆)alkylsulfonylamino(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₁-C₆)alkoxycarbonyl amino(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₂-C₉)heterocycloalkyloxycarbonylamino(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₂-C₉)heterocycloalkyl(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₂-C₉)heterocycloalkyl(C₁-C₆)alkylaminocarbonylamino(C₁-C₆)alkyl, (C₂-C₉)heterocycloalkyl(C₁-C₆)alkyl, ureido(C₁-C₆)alkylureido(C₁-C₆)alky
- 31. (Currently Amended) The compound of claim 20 e#21-wherein R⁵ is amino(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, (C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, (C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, acetylamino(C₁-C₆)alkyl), ((C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, (C₂-C₉)heterocycloalkyloxycarbonylamino(C₁-C₆)alkylsulfonylamino(C₁-C₆)alkyl, aminosulfonylamino(C₁-C₆)alkyl, (C₁-C₆)alkyl, (C₁-C₆)alkyl, (C₁-C₆)alkyl, (C₁-C₆)alkyl, (C₁-C₆)alkyl, aminosulfonylamino(C₁-C₆)alkyl, (C₁-C₆)alkyl).

USSN 10/660,052 Page 16 of 29 Amendment and Response to OA dated June 25, 2004

- (Currently Amended) The compound of claim 20 or 21-wherein R⁵ is cyanoguanidino(C₁-C₆)alkyl, (C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂(cyanoguanidino)(C₁-C₆)alkyl, (C₂-C₉)heterocycloalkyl(cyanoguanidino)(C₁-C₆)alkyl, (C₂-C₉)heteroaryl(cyanoguanidino)(C₁-C₆)alkyl, (C₂-C₉)heteroaryl(C₁-C₆)alkyl, (C₂-C₉)heterocycloalkyl(C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl, (C₂-C₉)heteroaryl(C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl, (C₁-C₆)alkyl, (C₁-C₆)alkyl, (C₁-C₆)alkyl, (C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂amino(C₁-C₆)alkyl, (C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl, (C₁-C₆)alkyl, (C₁-C₆)alkyl)₂aminocarbonyl(C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl) or ((C₁-C₆)alkyl)₂aminocarbonyl(C₁-C₆)alkyl(cyanoguanidino)(C₁-C₆)alkyl.
- (Currently Amended) The compound of claim 20 or 21-wherein R5 is (C2-33. C9)heterocycloalkylsulfonyl, amino(C1-C6)alkylaminosulfonyl, (C1-C6)alkylamino(C1- C_6)alkylaminosulfonyl, ((C_1 - C_6)alkyl)₂amino(C_1 - C_6)alkylaminosulfonyl, (C_2 -C9)heteroarylaminosulfonyl, ureido(C1-C6)alkylaminosulfonyl, (C1-C6)alkylureido(C1-C₆)alkylaminosulfonyl, ((C₁-C₆)alkyl)₂ureido(C₁-C₆)alkylaminosulfonyl, (C₁-C₆)alkylsulfonylamino(C₁-C₆)alkylaminosulfonyl, (C₁-C₆)alkoxycarbonylamino(C₁-C₆)alkylaminosulfonyl, (C₂-C₉)heterocycloalkyloxycarbonylamino(C₁-C₆)alkylaminosulfonyl, (C₂-C₉)heteroaryloxycarbonylamino(C₁-C₆)alkylaminosulfonyl, aminocarbonyl(C₁-C₆)alkylaminosulfonyl, cyanoguanidino(C₁-C₆)alkylaminosulfonyl, (C₂-C₉)heteroaryl(C₁-C₆)alkylaminosulfonyl, (C₂-C₉)heterocycloalkylaminosulfonyl, Other preferred compounds of formula I include those wherein R⁵ is halo(C₁-C₆)alkylaminocarbonyl, hydroxy(C₁-C₆)alkylureido, halo(C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkoxycarbonyl(C₁-C₆)alkylamino(C₁-C₆)alkyl, $hydroxy(C_1-C_6) alkylamino carbonylamino (C_1-C_6) alkyl, halo (C_1-C_6) alkylsul fonylamino (C_1-C_6) alkyl, halo (C_1-C_6) alkylsul fonylamino (C_1-C_6$ aminosulfonyl, (C₁-C₆)alkylaminosulfonyl, ((C₁-C₆)alkyl)₂aminosulfonyl, hydroxy(C₁- C_6)alkylaminosulfonyl, and $or(C_1-C_6)$ alkoxy(C_1-C_6)alkylaminosulfonyl.

USSN 10/660,052

Page 17 of 29